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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/713,687	11/15/2000	Stanley J. Watowich	122144-1008	5312

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EXAMINER
LI, BAO Q

ART UNIT	PAPER NUMBER
1648	11

DATE MAILED: 11/05/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/713,687	WATOWICH ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-7 and 49-65* is/are pending in the application.

4a) Of the above claim(s) *56-59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-7,49-55 and 60-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *56-59* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicants' amendment in response to the Office Action on Election/Restriction is noted. Claims 1-4 and 8-48 have been cancelled. New Claims 49-65 have been added. Claims 5-7 and 49-65 are pending.

Claims objection

The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 57-66 have been renumbered 56-65.

Election/Restrictions

1. In response to the Office Action on election/Restriction requirement, paper No. 8, Applicants elect with traverse of Group II, claims 5-7 in Paper No. 18 and ask to rejoin all newly added claims 49-65 into the elected group II. Applicants, however, did not distinctly and specifically point out the supposed errors in the restriction requirement; the election therefore, has been treated as an election without traverse (MPEP § 818.03(a)).

2. Regarding to the newly added claims 49-65, claims 49-55 and 65 are rejoined with the elected claims 5-7 because they are directed to a eukaryotic virus pseudo-nucleocapsid formed by a cell free in vitro self-assembly system. However, the claims 57-61 are not rejoined with the claims 5-7 because they are drawn to a virus pseudo-nucleocapsid with different structure characteristics and produced by using a vector in cell culture system. They should be restricted into another group. Hence, only claims 5-7, 49-55 and 60-65 are considered before the examiner.

3. Applicants are request to cancel the claims 56-59 drawn to the non-elected group.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 5-7, 49-55 and 60-65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claim 5 is unclear for recitation that the claimed virus pseudo-nucleocapsid comprising at least more a portion of a viral capsid polypeptide and a polynucleotide. First, the phrase "comprising at least " used here is a relative word, which fails to define the structural characteristics of the claimed product. Moreover, the metes and bounds of a portion of a viral capsid polypeptide and a polynucleotide are not defined. The claims are interpreted in light of the specification,; however, the specification does not teach what the definition of a portion of a portion of a viral capsid polypeptide and a polynucleotide are. If applicants wish to claim a particular viral pseudo-nucleocapsid made by a particular polypeptide and polynucleotide, please amend the claim by using more defined language, such as "consisting of" and a precise structures of the polypeptide and polynucleotide. This affects the dependent claims 6-7, 49-52 and 55.

7. Claims 49, 51, 52, 53, 54, 55, 63, 65 and 65 are indefinite for using a relative word of " comprising", which fails to define what the precise structure or component of each element contained in the claimed virus pseudo-nucleocapsid. Please clarify.

8. Claims 51, 52, 63 are vague and indefinite in that the metes and bounds of a recombinant polypeptide are not defined. The claims are interpreted in light of the specification; however, the specification does not teach what the definition of a recombinant polypeptide is and claim itself does not define what a recombinant polypeptide is. Therefore, the claims are considered indefinite.

9. Claim 52 is vague in that the metes and bounds of functional homologous are not defined. The claim is interpreted in light of the specification; however, the specification does not teach what the definition of the "functional homologous" is.

10. Claim 54 is unclear in that the recited "truncations" are not defined. The claim is interpreted in light of the specification; however, the specification does not teach what the definition of the "truncations" is.

11. Claim 65 is vague and indefinite in that the metes and bounds of a portion of a hepatitis C virus genome are not defined. The claim is interpreted in light of the specification; however, the specification does not teach what the definition of a portion of a hepatitis C virus genome is and

nor does the claim define what a portion of a hepatitis C virus genome is . Therefore, the claim is considered indefinite.

Claim Rejections - 35 USC § 112

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 5-7, 49-56 and 61-65 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for having a HCV pseudo-nucleocapsid made by incubating the mixture of HCV core protein encoded by SEQ ID NO: 1 and tRNA in an in vitro array, does not reasonably provide enablement for having any or eukaryotic virus pseudo-nucleocapsid comprising any or all a portion of viral capsid polypeptide and a polynucleotide formed in any or all in vitro system. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The test of scope of the enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art would undue experimentation (See United States v. Theketronic Inc., 8USPQ2d 1217 (fed Cir. 1988). Whether undue experimentation is required is not based upon a single factor but rather a conclusion reached by weighting many factors. Theses factors were outlined in Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and gain in re Wands, 8USPQ2d 1400 (Fed. Cir. 1988).

1) & 2) State of art and Unpredictability.

A viral like particle of an empty protein capsid can be produced by a cell free sell-assembly system. However, only every virus and any protein or protein part is able to form a self-assembly virus particle as evidenced by Platt et al. (Pro. Natl. Acad. Sci. USA 1994, Vol. 91, pp. 4594-4598). They teach that HIV gag protein p55 is able to form a virus like particle in a cell free system, but is require the seven-amino acid sequence located between the two Cys-His arrays in the nucleocapsid region (See entire document).

3) & 4) Number of working examples and Amount of guidance.

Specification does not present working examples of any portion of a viral polypeptide plus any or all polynucleotides are able to assembly a spherical pseudo-nucleocapsid in such an in vitro array method.

Specification is deficient for teaching that other virus capsid protein or portion of any other virus capsid proteins plus tRNA molecules or other polynucleotide are able to form a spherical pseudo-nucleocapsid in any or all in vitro system.

Specification lacks of adequate teaching about what other recombinant polynucleotide or genome of HCV are required for the pseudo-type capsid formation in an in vitro array

5). Scope of the claimed invention.

The scope of the claimed invention read on a eukaryotic virus pseudo-nucleocapsid made by any or all portion of a virus polynucleotide plus any or all polynucleotide assembled in any or all in vitro setting system.

6) & 7) Nature of the invention and Level of the skill in the art.

The invention involves a high technology and undue experimentation to test any portion of a viral polypeptide plus a polynucleotide to assemble a pseudo-nucleocapsid in vitro.

Given the above analysis of the factors, which the courts have determined, are critical in asserting whether a claimed invention is enabled, it must be considered that the skilled artisan would have had to conduct undue and excessive experimentation in order to practice the claimed invention.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 5, 50, 51 and 61-63 are rejected under 35 U.S.C. 102(b) as being anticipated by Spearman et al. (J. Virol. 1996, Vol. 70, pp. 8187-8194).

16. Spearman et al. teach that a eukarytoc virus pseudo-capsid made by a recombinant HIV gag protein P55 are formed in an in vitro reticulaocyte lysate translation system. This system contains RNA, DNA, ribosome as well as the gag protein. Under the microscope, the HIV p55 pseudo- capsids were identified as spherical capsid particles (See entire document). Therefore, the claimed invention is anticipated by the cited reference.

17. Claims 5, 50, 51 and 61-63 are rejected under 35 U.S.C. 102(b) as being anticipated by Lingappa et al. (J. Cell Biology. 1994, Vol. 125, pp. 99-111).

18. Lingappa et al. teach that a eukarytoc virus pseudo-capsid of HBV core is formed in an in vitro translation system. The pseudo-capsid is found indistinguishable from the authentic viral capsid by four criteria: velocity sedimentation, buoyant, density, proteanase resistance and electron microscopic appearance. This system requires the HBV core protein cDNA, SP6 polymerase, wheat germ extract and a 60kD protein related to the chaperonin complex polypeptide (TCP-1) (See entire document). Therefore, the claimed invention is anticipated by the cited reference.

19. Claims 5-7, 49, 51 and 61-63 are rejected under 35 U.S.C. 102(b) as being anticipated by Sugrue et al. (J. General Virol. 1997, Vol. 78, pp. 1861-1866).

20. Surgue et al. teach that a pseudo type of viral like particle comprising Denue virus capsid core protein C plus other proteins, such as E and M are assembled in a yeast cell system. The Denue virus is a flavivirus and the pseudo-virus like particle comprises capsid core protein and other recombinant protein as well as polynucleotide of Denue virus, such as E and M (See entire document). Therefore, the claimed invention is anticipated by the cited reference.

21. Claims 5-7, 49, 51, 52, 53, 54, 55 and 60-65 are rejected under 35 U.S.C. 102(b) as being anticipated by Baumert et al. (J. Virol. 1998, Vol. 72, pp. 3827-3836).

22. Baumert et al. teach that a pseudo type of HCV viral like particles comprising HCV capsid core protein and other HCV polypeptide and polynucleotide are assembled in an in vitro insect cell system. The viral like particle also comprise other HCV genome, such as HCV E1 and E2 proteins (See entire document). Therefore, the claimed invention is anticipated by the cited reference.

23. Claims 5-7, 49, 51 and 60-62 are rejected under 35 U.S.C. 102(b) as being anticipated by Thomsen et al. (J. General Virol. 1992, Vol. 73, pp. 1819-1824).

24. Thomsen et al. teach that a pseudo-type of feline leukemia virus (FeLV) like particles comprising a recombinant FeLV capsid gag and other recombinant protein of FLV envelope protein gp85 are assembled in an in vitro insect cell system. The pseudo viral like particle of FeLV appears under the electron microscopic similar to those of authentic FeLV virions (See entire document). Therefore, the claimed invention is anticipated by the cited reference.

25. Claims 5-7, 49 and 51 are rejected under 35 U.S.C. 102(b) as being anticipated by Vladimir et al. (Virol. 1993, Vol. 192, pp. 38-51).

26. Vladimir et al. teach a pseudo type of viral like particle made by Denue virus capsid protein C plus other proteins, such as pre-M-E as well as NS2B etc. The pseudo virus like particles are assembled in human TK1143B cell line and Hela T4 cells, which is a mammalian host cell system. The Denue virus is a flavivirus and the pseudo-virus like particle comprises capsid C protein and other recombinant protein as well as polynucleotide (See entire document). Therefore, the claimed invention is anticipated by the cited reference.

27. Claims 5, 6, 7, 49-52, 54-55 and 61-65 are rejected under 35 U.S.C. 102(b) as being anticipated by Yusui et al. (J. Virol. 1998, Vol. 72, pp. 6048-6055).

28. Yusui et al. teach a HCV capsid particle formed in vaccinia virus expressing system and mammalian cells stably transformed with HCV cDNA encoding HCV core protein. The particle is pseudo capsid particle because is formed in an in vitro system by transformation of only part of the HCV genome comprising the HCV core and other polypeptide or polypeptides. Some of the particle was observed as a spherical comprising the wild type or truncated form of HCV core protein. Therefore, the claimed invention is anticipated by the cited reference.

29. Claims 5, 6, 7, 49-52, 54-55 and 61-65 are rejected under 35 U.S.C. 102(b) as being anticipated by Liang et al. (WO 98/21338A1).

30. Liang et al. disclosed an isolated hepatitis C virus like particle comprising HCV capsid core protein and E1 and E2 proteins. The particle is produced by transfeting the insect cells with cDNA encoding HCV core, E1 and E2 proteins (See entire document and claims 1-20). The particles are observed under the electron microscope as a spherical (Fig. 1-3). Therefore, the claimed invention is anticipated by the cited reference.

31. Claims 5, 6, 49-51, and 61-63 are rejected under 35 U.S.C. 102(b) as being anticipated by Wengler et al. (Virol. 1982, Vol. 118, pp. 401-411).

32. Wengler et al. disclosed a method for making a pseudo-nucleocapsid in vitro and the pseudo-nucleocapsid comprising flavivirus Sindbis virus core protein and other viral RNA, such as tRNA as well as other single-stranded nucleic acids. The pseudo-nucleocapsids appeared under the electron microscope have same spherical morphology to the authentic viral core (See entire document). Therefore, the claimed invention is anticipated by the cited reference.

Claim Rejections - 35 USC § 102

33. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

34. Claims 5, 49-51 and 60-63 are rejected under 35 U.S.C. 102(a) as being anticipated by Bother et al. (Nature Structural Biology, 1999, Vol. 6, pp. 114-116).

Bother et al. teach that a speudo-virus like particle made by both wild type and truncated capsid coat protein of Flock house virus (FHV) in combination with cellular protein-RNA is produced in a baculovirus expression system, which produce virus like particles (VLPs) that are morphologically indistinguishable from authentic FHV except that they contain cellular RNA instead of the viral genomic RNA. Crystallographic comparisons of authentic FHV particles and VLPS show that they are indistinguishable (See entire document). Therefore, the claimed invention is anticipated by the cited reference.

35. Claims 5, 6, 49-51 and 61-63 are rejected under 35 U.S.C. 102(a) as being anticipated by Tellingghuisen et al. (J. Virol. 1999, Vol. 73, pp. 5309-5319).

36. Tellingghuisen et al. that a pseudo-type virus like particle of alphavirus, Sindbis virus (SINV) can be assembled in an in vitro system. The pseudo-type capsid particle is made by mixing equal volumes of prewarmed capsid protein CP of SINV and oligonucleotide. The CP binds to genomic RNA and rapidly assembles into a nucleocapsid core (NC) to form a SINV core like particles (CLPs). Both wild type and truncated recombinant CP produced by the plasmid in E Coli cells are able to produce the CPLs in the in vitro array. This in-vitro-assembly

of CLPs requirs both virus specific RNA and non-specific RNA, especially the yeast tRNA was found to serve as a substrate for in vitro CPL formation. They conclude that the examination of assembly core particle by electron microscopy, gradient sedimentation and agarose gel assay suggested that in vitro-assembled cores were of a regular size and shape and appeared quit similar to native cytoplasmic cores or virus-purified cores (See entire document, especially the Fig. 3 and Table 1 on page 5314 and lines 6-10 on left col. of page 5317). Therefore, the claimed invention is anticipated by the cited reference.

37. Claims 5, 6, 7, 49-52, 54, 55 and 61-65 are rejected under 35 U.S.C. 102(a) as being anticipated by Falco et al. (Tissue & Cell, 1999, Vol. 31, pp. 117-125).

38. Facol. Et al. teach that a speudo HCV core particle comprising the first 399 NH2-ternimal amino acids of HCV polypeptide (C-E1. 399 polypeptide) are formed in Pichia pastoris yeast. They concluded that the like mammalian cell lines, the P. pastori yeast is an appropriate host for assembly the VLP of HCV comprising the HCV core and envelope protein as well as both cellular and virus RNA molecules (See entire document). Therefore, the claimed invention is anticipated by the cited reference.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 703-305-1695. The examiner can normally be reached on 8:00 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Bao Qun Li November 3, 2002

JAMES HOUSEL 11/3/02
SUPERVISORY PATENT EXAMINER
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